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JSP 120 #37



U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER

Docket Number:
1247/9

Application Number
726,178

Filing Date
4/23/85

Examiner

Art Unit

Patent Number
4,692,435

Issue Date
September 8, 1987

Invention Title
Mucopolysaccharide Composition Having a
Regulatory Action on Coagulation, Medicament
Containing Same and Process of Preparation

Inventor(s)
Lormeau et al.

Address to:
Commissioner of Patents and Trademarks
Washington D.C. 20231
Box Pat. Ext.

SIR:

Please find enclosed an Amended Application for Extension of Patent Term Under 35 U.S.C. 156 which is being filed in connection with the above-referenced patent.

This paper amends section 8 of the original application to specifically state that a receipt for maintenance fee payment is provided as Exhibit C. It further amends section 10 to include both the date that the NDA was initially submitted (July 26, 1991) and the effective date of the NDA submission (December 31, 1991).

The amended application also corrects the calculation of the length of extension of the patent term claimed by the applicant in section 12 of the original application. In particular, the calculations in subparagraphs (h), (j), (l), (m) and (n) have been amended on page 10. The amended section 12 also claims, in the alternative, the length of extension computed by the Federal Drug Administration and published at 58 Fed. Reg. 62,356 (1993).

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on

Date 12-21-93 Atty's Reg. # 25,054

Atty's Signature


Albert J. Breneisen
KENYON & KENYON
ALBERT J. BRENEISEN

94 JUN -5 CITE: 322

The applicant wishes to bring to the attention of the Patent Office that it will seek a redetermination by the Federal Drug Administration ("FDA") of the length of extension. In particular, the length of the testing period should be calculated from the effective date of the IND up to the date the NDA application was initially submitted (July 26, 1991) and not up to the date the NDA application was deemed effective by the FDA (December 31, 1991).

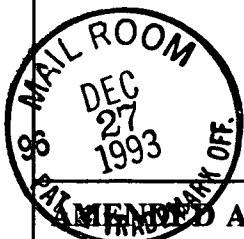
Respectfully submitted,

Dated: December 20, 1993


Albert J. Breneisen
(Reg. No. 25,054)

KENYON & KENYON
One Broadway
New York, New York 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile)

Please charge any fees to Deposit Account No. 11-0600.



U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

**AMENDED APPLICATION
FOR EXTENSION OF PATENT TERM
UNDER 35 U.S.C. 156**

Docket Number:
1247/9

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726,178

Filing Date
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United States Postal Service as first class mail in an envelope addressed
to: Commissioner of Patents and Trademarks, Washington, D. C. 20231, on

Date 12-21-93 Atty's Reg. # 25,054

Atty's Signature

Albert J. Breneman
KENYON & KENYON

Choay, S.A., assignee and owner of the entire 100% interest in patent
4,692,435 (the "'435 patent") submits this request for patent term extension for the
'435 patent.

(1) The approved product is LOVENOX® enoxaparin, a low molecular weight
heparin product, containing a mixture of lower molecular weight fractions in the
range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of
a molecular weight in the range of about 4,000 to about 10,000 daltons as determined
by gel permeation chromatography.

(2) Regulatory review of LOVENOX® enoxaparin occurred under 21 U.S.C. § 355.

(3) the LOVENOX® product received permission for commercial marketing under 21
U.S.C. § 355 on March 29, 1993.

(4) The only active ingredient in the LOVENOX® product is enoxaparin. Enoxaparin
has not been previously approved for commercial marketing or use under the Federal
Food, Drug and Cosmetic Act, the Public Health Service Act, or the Virus-Serum-
Toxin Act.

(5) This application is being submitted by the owner of the '435 patent, Choay S.A.,
within the sixty day period permitted for submission pursuant to 37 CFR § 1.720(f).
The last day on which the application could be submitted is May 28, 1993.

(6) The patent for which an extension is being sought is U.S. 4,692,435, issued September 8, 1987. The inventors were Jean-Claude Lormeau, Jean Goulay, and Jean Choay. The '435 patent currently expires December 4, 2001.

(7) A copy of the '435 patent is attached hereto as Exhibit A.

(8) A copy of a terminal disclaimer, disclaiming the terminal portion of the '435 patent is attached hereto as Exhibit B. No certificates of correction or reexamination certificates have been issued. A copy of a receipt for maintenance fee payment is provided as Exhibit C.

(9) The '435 patent claims the approved product, methods of using the approved product, and methods of making the approved product. The applicable patent claims and the manner in which each applicable claim reads on the approved product or method of using the approved product follows:

Claim 18. Heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and the physiologically acceptable salts thereof.

LOVENOX® enoxaparin contains heparinic mucopolysaccharide fractions having

- (a) The Lovenox® product package insert indicates that, at minimum, 68% of the LOVENOX® mucopolysaccharides have molecular weights between 2000 and 8000 daltons; no more than 15% have molecular weight greater than 8000 daltons, and no more than 20% have molecular weights less than 2,000 daltons. A study on the LOVENOX® product by Choay indicated that 90% of the mucopolysaccharides had molecular weights between 1900 and 8500 daltons, and fewer than 1% had molecular weights greater than 11,000 daltons, or less than 1600 daltons, as measured by gel permeation chromatography;
- (b) A study on the LOVENOX® product by Choay indicated that
 - (i) roughly half of the mucopolysaccharides had molecular weight between 10333 and 4096 daltons, and roughly half have molecular weight between 4096 and 2050 daltons;
 - (ii) it exhibited a Yin-Wessler of at least 40, namely approximately 240-250 U/mg;

- (iii) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, namely about 4.36;
- (c) The LOVENOX® product has improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin.
- (d) The LOVENOX® mucopolysaccharide fractions are sodium salts.

Claim 19. The heparinic mucopolysaccharide fractions of claim 18 wherein the lower molecular weight fractions are free of nucleic acids.

LOVENOX® enoxaparin is substantially free of nucleic acids.

Claim 21. The heparinic mucopolysaccharides of claim 18 wherein the molecular weight is not in excess of about 8,000 daltons.

See the comment above on the molecular weight of LOVENOX® mucopolysaccharides.

Claim 31. The heparinic mucopolysaccharides of claim 18 wherein fractions have a molecular weight range of about 2,000 to about 8,000.

See the comment above on the molecular weight of LOVENOX® mucopolysaccharides.

Claim 32. The heparinic mucopolysaccharide fractions of claim 19 which are soluble in an aqueous-alcoholic medium, and insoluble in pure alcohol.

The LOVENOX® enoxaparin heparinic mucopolysaccharide fractions are soluble in an aqueous-alcoholic medium, and insoluble in pure alcohol.

Claim 11. A therapeutic composition for controlling thrombosis and decreasing hemorrhaging and of blood hypercoagulation risks which comprises a therapeutically acceptable carrier and heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, and the physiologically acceptable

salts thereof, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower and slower than that of heparin.

The LOVENOX® product is a therapeutic composition for controlling thrombosis and decreasing hemorrhaging and of blood hypercoagulation risks. It contains a therapeutically acceptable carrier. The composition of the mucopolysaccharide fractions is described above with respect to claim 18.

Claim 12. The therapeutic composition of claim 11 which is a solution.

The LOVENOX® product is marketed as a solution.

Claim 13. The therapeutic composition of claim 12 wherein the heparinic mucopolysaccharides fractions are in solution in a concentration of about 1,000 to 100,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the solution has a concentration of roughly 25,000 Yin-Wessler units per mL.

Claim 14. The therapeutic composition of claim 13 which is a solution of the mucopolysaccharides in a concentration of about 5,000 to about 50,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the solution has a concentration of roughly 25,000 Yin-Wessler units per mL.

Claim 15. The solution of claim 12 which is apyrogenic.

The LOVENOX® product is apyrogenic.

Claim 16. The solution of claim 15 which is sterile.

The LOVENOX® product is sterile.

Claim 4. A therapeutic method for controlling thrombosis and decreasing blood hypercoagulation and hemorrhaging risks in a

patient which comprises administering to the patient in an antithrombotic effective amount, a composition which comprises a therapeutically acceptable carrier and heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, and the physiologically acceptable salts thereof, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and said method controlling thrombosis by selectively inhibiting coagulation factor Xa while also having a whole anticoagulation effect which is slower and lower than that of heparin.

The LOVENOX® therapeutic composition has been approved by the FDA for use in a method for prevention of deep vein thrombosis, which may lead to pulmonary embolism following hip replacement surgery, via injection of LOVENOX® solution. The composition has been described above under claim 18.

Claim 5. The method of claim 4 wherein the administration is by injection or infusion to the patient.

The LOVENOX® product has been approved by the FDA for administration by injection.

Claim 6. The method of claim 5 wherein the administration by injection is sub-cutaneous.

LOVENOX® has been approved by the FDA for administration by injection. It is not indicated for intramuscular administration. It may be administered sub-cutaneously.

Claim 7. The method of claim 6 wherein the dosage administered sub-cutaneously is from about 1,000 to about 25,000 Yin-Wessler units per ml.

The LOVENOX® product is marketed in solution. Choay S.A. has determined that the concentration is roughly 25,000 Yin-Wessler units per mL.

Claim 47. The therapeutic method of claim 4 wherein the patient is exposed to risks of hypercoagulability.

LOVENOX® enoxaparin is indicated for patients who are exposed to risks of hypercoagulatability.

Claim 33. A therapeutic composition which presents less risks than heparin of blood hypercoagulation and of a host hemorrhaging, which composition has improved antithrombotic activity (anti-Xa activity) and improved selectivity with respect to anti-Xa activity than heparin in vivo and a lower and slower anticoagulation activity than heparin, and which composition comprises a therapeutically acceptable carrier and an antithrombotic effective amount of heparinic mucopolysaccharide fractions having constituents of a molecular weight not in excess of about 10,000 daltons, which fractions have (1) a mixture of lower molecular weight fractions in the range of about 2,000 to about 4,000 daltons with higher molecular weight fractions of a molecular weight in the range of about 4,000 to about 10,000 daltons, (2) a Yin-Wessler of at least 40, and (3) a ratio of Yin-Wessler to USP titer in the range of 3 to 5, which mixture of fractions have improved antithrombotic activity in vivo which is higher than that of heparin and a whole anticoagulation activity lower than that of heparin, and the physiologically acceptable salts thereof.

The LOVENOX® product is a therapeutic composition which presents less risks than heparin of blood hypercoagulation and of a host hemorrhaging. The composition and properties of LOVENOX® are discussed above with respect to claim 18.

Claim 35. The therapeutic composition of claim 33 in which the molecular weight of the heparinic mucopolysaccharides is not in excess of about 8,000 daltons.

See comment (a) to claim 18 for the molecular weight distribution of LOVENOX® enoxaparin.

(10) The relevant dates and information pursuant to 35 USC 156(g) in order to enable the Secretary of Health and Human Services to determine the applicable regulatory review period is:

IND number: 31532
IND effective date: May 19, 1988

NDA number 20-164
NDA submission date: July 26, 1991
NDA effective date: December 31, 1991
NDA approval date: March 29, 1993

(11) The LOVENOX® NDA was approved by the FDA on an IND and NDA filed by Rhone-Poulenc Rorer Pharmaceuticals, Inc. ("RPRP"), the licensee of the '435 patent. As a brief description of the significant activities undertaken by Rhone-Poulenc Rorer Pharmaceuticals, Inc., during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities, attached hereto as Exhibit D is a brief chronology of the communications with the FDA during the regulatory review period ending with approval on March 29, 1993.

(12) In the opinion of the applicant, the '435 patent is eligible for patent term extension under 35 USC 156 because

- (a) 35 U.S.C 156(a)
The '435 patent claims a product, and a method of using a product.
- (b) 35 U.S.C 156(a)(1)
The term of the '435 patent has not expired before submission of this application.
- (c) 35 U.S.C. 156(a)(2)
The term of the '435 patent has never been extended.
- (d) 35 U.S.C. 156(a)(3)
The application for extension is submitted by Choay S.A., the owner of record in accordance with the requirement of 35 U.S.C. 156(d) and rules of the U.S. Patent and Trademark Office.
- (e) 35 U.S.C. 156(a)(4)
The LOVENOX® product has been subjected to a regulatory review period before its commercial marketing or use.
- (f) 35 U.S.C. 156(a)(5)(A)
The commercial marketing or use of the LOVENOX® product, after the regulatory review period is the first permitted commercial marketing or use of LOVENOX® product under the provision of the Federal Food Drug and Cosmetic Act (21 U.S.C. 355) under which such regulatory review period occurred.
- (g) 35 U.S.C. 156(c)(4)
No other patent has been extended for the same regulatory review period for the LOVENOX® product.

The length of extension of the patent term of the '435 patent claimed by applicant is 1,195 days, until March 13, 2005. The length of the extension was determined pursuant to 37 C.F.R. 1.775 as follows:

- (a) 1164 The number of days in the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food Drug and Cosmetic Act became effective for the approved product (May 19, 1988) and ending on the date the application was initially submitted for such product under those sections or under section 351 of the Public Health Service Act (July 26, 1991); (37 C.F.R. 1.775(c)(1))

- (b) 613 The number of days in the period beginning on the date the application was initially submitted for the approved product under section 351 of the Public Health Service Act, subsection (b) of section 505 or section (507) of the Federal Food, Drug, and Cosmetic Act (July 26, 1991) and ending on the date such application was approved under such section (March 29, 1993). (37 C.F.R. 1.775(c)(2))
- (c) 1777 The sum of (a) and (b). This is the regulatory review period. (37 C.F.R. 1.775(c))
- (d) 0 the number of days in the regulatory review period which were on and before the '435 patent issued (September 8, 1987). (37 C.F.R. 1.775(d)(1)(i))
- (e) 0 the number of days in the regulatory review period during which it is determined under 35 U.S.C 56(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence.¹ (37 C.F.R. 1.775(d)(1)(ii))
- (f) 0 the sum of (d) and (e).
- (g) 1777 (c) - (f). (37 C.F.R. 1.775(d)(1)(ii))
- (h) 1195 1/2 of (a) + (b). (37 C.F.R. 1.775(d)(1)(iii))
- (i) 12/04/2001 The original term of the '435 patent, shortened by any terminal disclaimer.
- (j) 03/13/2005 The original term of the patent as shortened by any terminal disclaimer plus the number of days in (h). (37 C.F.R. 1.775(d)(2))
- (k) 03/29/2007 The date of approval of the application under section 351 of the Public Health Service Act, or subsection (b) of section 505 or section 507 of the Federal Food, Drug and Cosmetic Act plus 14 years. (37 C.F.R. 1.775(d)(3))
- (l) 03/13/2005 The earlier of (j) and (k). (37 C.F.R. 1.775(d)(4))
- (m) 12/04/2006 (i) plus 5 years. (37 C.F.R. 1.775(d)(5)(i))
- (n) 03/13/2005 The earlier of (l) and (m). (37 C.F.R. 1.775(d)(5)(ii))

1. There has been no such determination. To the best of applicant's knowledge, RPRP was diligent during the regulatory review period.

Alternatively, the length of extension of the patent term of the '435 patent claimed by applicant is 1,116 days, until December 24, 2004, per the initial determination of the Food and Drug Administration as published at 58 Fed. Reg. 62,356 (1993). The length of the extension was determined as follows:

- (a) 1322 The number of days in the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food Drug and Cosmetic Act became effective for the approved product (May 19, 1988) and ending on the date the application was initially submitted and effective for such product under those sections or under section 351 of the Public Health Service Act (December 31, 1991); (See 37 C.F.R. 1.775(c)(1); Determination of Regulatory Review Period for Purposes of Patent Extension; Lovenox®, 58 Fed. Reg. 62,356 (1993))
- (b) 455 The number of days in the period beginning on the date the application was initially submitted and effective for the approved product under section 351 of the Public Health Service Act, subsection (b) of section 505 or section (507) of the Federal Food, Drug, and Cosmetic Act (December 31, 1991) and ending on the date such application was approved under such section (March 29, 1993). (See 37 C.F.R. 1.775(c)(2); Determination of Regulatory Review Period for Purposes of Patent Extension; Lovenox®, 58 Fed. Reg. 62,356 (1993))
- (c) 1777 The sum of (a) and (b). This is the regulatory review period. (37 C.F.R. 1.775(c))
- (d) 0 the number of days in the regulatory review period which were on and before the '435 patent issued (September 8, 1987). (37 C.F.R. 1.775(d)(1)(i))
- (e) 0 the number of days in the regulatory review period during which it is determined under 35 U.S.C 56(d)(2)(B) by the Secretary of Health and Human Services that applicant did not act with due diligence.² (37 C.F.R. 1.775(d)(1)(ii))
- (f) 0 the sum of (d) and (e).
- (g) 1777 (c) - (f). (37 C.F.R. 1.775(d)(1)(ii))

2. There has been no such determination. To the best of applicant's knowledge, RPRP was diligent during the regulatory review period.

- (h) 1116 1/2 of (a) + (b). (37 C.F.R. 1.775(d)(1)(iii))
- (i) 12/04/2001 The original term of the '435 patent, shortened by any terminal disclaimer.
- (j) 12/24/2004 The original term of the patent as shortened by any terminal disclaimer plus the number of days in (h). (37 C.F.R. 1.775(d)(2))
- (k) 03/29/2007 The date of approval of the application under section 351 of the Public Health Service Act, or subsection (b) of section 505 or section 507 of the Federal Food, Drug and Cosmetic Act plus 14 years. (37 C.F.R. 1.775(d)(3))
- (l) 12/24/2004 The earlier of (j) and (k). (37 C.F.R. 1.775(d)(4))
- (m) 12/04/2006 (i) plus 5 years. (37 C.F.R. 1.775(d)(5)(i))
- (n) 12/24/2004 The earlier of (l) and (m). (37 C.F.R. 1.775(d)(5)(ii))

(13) The applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services or the Secretary of Agriculture any information which is material to the determination of entitlement to the extension sought.

(14) The proscribed fee for receiving and acting upon the original application for extension filed on May 24, 1993 pursuant to 37 C.F.R. 1.20(j) was charged to deposit account 11-0600. Please charge any additional fees for receiving and acting upon this amended application for patent term extension to deposit account 11-0600.

(15) Please address inquiries and correspondence to the undersigned.

(16) A triplicate of these application papers is submitted herewith.

- (17) The following declaration is submitted herewith in compliance with the requirements of 37 C.F.R. § 1.740(b):


DECLARATION

The undersigned, Attorney for Choay, S.A., which is the applicant submitting this amended application for patent term extension of United States Patent No. 4,692,435 hereinabove referred to as the '435 patent, in compliance with the requirements of 37 C.F.R. § 1.740(b)(1), hereby avers as follows:

1. He is a patent attorney authorized to practice before the United States Patent and Trademark Office (Reg. No. 25,054) and he is authorized to represent Choay, S.A. in this amended application of patent term extension of the '435 patent and to transact all business in the United States Patent and Trademark Office in connection therewith;
2. He has reviewed and understands the contents of this amended application for patent term extension of the '435 patent;
3. He believes that the '435 patent is subject to patent term extension pursuant to the provisions of 37 C.F.R. § 1.710;
4. He believes that the extension of the length claimed in this amended application for patent term extension of the '435 patent is justified under 35 U.S.C. § 156 and the applicable regulations relating thereto; and
5. He believes that the '435 patent which is the subject of this amended application for patent term extension meets the conditions for patent term extension as set forth in 37 C.F.R. § 1.720.

Respectfully submitted,

Dated: December 20, 1993


Albert J. Breneisen
Reg. No. 25,054

Steven J. Lee
Reg. No. 31,272

Attorneys for Applicant
Choay, S.A.

KENYON & KENYON
One Broadway
New York, N.Y. 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile)

Exhibit A

United States Patent [19]
Lormeau et al.

[11] Patent Number: **4,692,435**
[45] Date of Patent: * **Sep. 8, 1987**

[54] **MUCOPOLYSACCHARIDE COMPOSITION
HAVING A REGULATORY ACTION ON
COAGULATION, MEDICAMENT
CONTAINING SAME AND PROCESS OF
PREPARATION**

[75] Inventors: **Jean-Claude Lormeau,
Maromme-la-Maine; Jean Goulay,
Oissel; Jean Chuay, Paris, all of
France**

[73] Assignee: **Chuay, S.A., Paris, France**

[*] Notice: The portion of the term of this patent
subsequent to Dec. 4, 2001 has been
disclaimed.

[21] Appl. No.: **726,178**

[22] Filed: **Apr. 23, 1985**

Related U.S. Application Data

[63] Continuation of Ser. No. 204,505, Nov. 5, 1980, abandoned.

[30] Foreign Application Priority Data

Nov. 6, 1978 [FR] France 78 31357
Jul. 20, 1979 [FR] France 79 18873

[51] Int. Cl.⁴ **A61K 31/725; C08B 37/10**

[52] U.S. Cl. **514/56; 536/21**

[58] Field of Search **536/21; 514/56**

References Cited

U.S. PATENT DOCUMENTS

4,168,377 9/1979 Choay et al. 424/183
4,175,182 11/1979 Schmier 536/21
4,281,108 7/1981 Fussi 424/183
4,303,651 12/1981 Landahl et al. 424/183
4,315,923 2/1982 Takacs et al. 424/183
4,486,420 12/1984 Lormeau et al. 536/21

Primary Examiner—Johnnie R. Brown

Attorney, Agent, or Firm—Weiser & Stapler

[57] ABSTRACT

The invention pertains to a mucopolysaccharide fraction obtainable from heparin or from fractions including heparinic constituents of molecular weights from 2000 to 50,000, which has a Yin-Wessler titer which is high relative to the USP titer. It contains components whose molecular weights are less than 10,000, particularly oligosaccharides in the area of 2000-3000, comprising from 8 to 12, notably 10 monosaccharide units, among which glucosamine units whose primary positions are sulphated. The last mentioned oligosaccharides include one N-acetyl-glucosamine unit per two units of 2-O-sulphate iduronic acid and per two N-sulphate-glucosamine units, the other saccharide units being of a different nature and including distinct substituents.

48 Claims, 15 Drawing Figures

2201479P/0257A/GW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of :
JEAN CLAUDE LORMEAU ET AL : Group Art Unit: 125
Serial No 204,505 : Examiner: J.R. Brown
Filed: November 6, 1980 : 703-557-3920
For a Patent for :
MUCOPOLYSACCHARIDE COMPOSITION :
HAVING A REGULATORY ACTION :
ON COAGULATION, MEDICAMENT :
CONTAINING IT AND PROCESS :
FOR PREPARING IT : January 31, 1984

TERMINAL DISCLAIMER UNDER 37 CFR 1.321(b)

Hon. Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Choay S.A. of 48 Theophile Gautier 75782 Paris, Cedex
16 (France) the owner of record of application Serial No.
204,505 filed November 6, 1980 and of application Serial No.
301,611 filed September 14, 1981, as evidenced by the
assignments recorded under Reel 3707 Frame 791 and Reel 3932
Frame 304, respectively, does hereby disclaim the terminal part
of any patent granted on application Serial No. 204,505 which
would extend beyond the expiration date any patent granted on
application Serial No. 301,611, if the latter patent is granted
first.

Choay S.A. hereby agrees any patents so granted on
said application shall be enforceable only for and during such
period that the legal title to said patents shall be the same.

This agreement shall run with any patent(s) granted on the above-said application and shall be binding upon the grantee, its successors or assigns.

CHOAY S.A.

by

Willaime
Title: General Manager
P. Willaime

Exhibit C


**UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office**

 Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D. C. 20231

75M1

 GERARD J. WEISER, ESQ.
WEISER & STAPLER
SUITE 500
230 S. 15TH STREET
PHILADELPHIA, PENNSYLVANIA 19102

 DATE MAILED
05/27/93

MAINTENANCE FEE STATEMENT

The data shown below is from the records of the Patent and Trademark Office. If the maintenance fees and any necessary surcharges have been timely paid for the patents listed below, the notation "PAID" will appear in column 10, "status" below.

If a maintenance fee payment is defective, the reason is indicated by code in column 10, "status" below. An explanation of the codes appears on the reverse of the Maintenance Fee Statement. **TIMELY CORRECTION IS REQUIRED IN ORDER TO AVOID EXPIRATION OF THE PATENT. NOTE 37 CFR 1.377. THE PAYMENT(S) WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION. IF PAYMENT OR CORRECTION IS SUBMITTED DURING THE GRACE PERIOD, A SURCHARGE IS ALSO REQUIRED. NOTE 37 CFR 1.20(k) and (l).**

If the statement of small entity status is defective the reason is indicated below in column 10 for the related patent number. **THE STATEMENT OF SMALL ENTITY STATUS WILL BE ENTERED UPON RECEIPT OF ACCEPTABLE CORRECTION.**

TM IBR	PATENT NUMBER	FEE CDE	FEE AMOUNT	SUR CHARGE	SERIAL NUMBER	PATENT DATE	FILE DATE	PAY YR	SML ENT	STAT
1	4,692,435	173	830	----	06/726,178	09/08/87	04/23/85	04	NO	PAID

Exhibit D

Rhone-Poulenc Rorer Central Research
Regulatory Affairs

APPLICATION CHRONOLOGY REPORT
Report Cover Page

Run Date: 05/05/93
User: lngres_prod

Selection Criteria

App Number: 20164

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93 App Num: 20164 Type: NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Route of Admin.: SU Dosage Form: SOLUTION 30 mg
Generic Name: enoxaparin

CONTENT Name/Description		Content Comments	
COMM DATE	COMM TYPE	Details	
26-JUL-91	ORIGINAL SUBMISSION	CLINICAL PRO#: STUDY INV NAME:	
05-AUG-91	GENERAL CORRESP FROM FDA	OTHER N/A	FDA ACKNOWLEDGED RECEIPT OF ORIGINAL NDA ON 29-JUL-91
20-SEP-91	GENERAL CORRESP FROM FDA	OTHER N/A	FDA COMMENTS AFTER PRELIMINARY REVIEW OF ORIGINAL NDA SUBMISSION
15-OCT-91	GENERAL CORRESP TO FDA	OTHER N/A	CHANGE OF ADDRESS
01-NOV-91	AMENDMENT	OTHER N/A	RESPONSE TO 20-SEP-91 FDA LETTER INDICATING REFUSAL TO FILE. INFO FOR DISCUSSION AT 13-NOV-91 INFORMAL CONFERENCE
15-NOV-91	MEETING MINUTES	OTHER N/A	INFORMAL CONFERENCE TO DISCUSS THE REASONS THE NDA WAS NOT ACCEPTED FOR FILING
10-JAN-92	PHONE CALL	PRECLINICAL STUDY#: SPECIES: RTS. ADMIN: DURATION:	MS. COLLIER RELAYED THE CSO'S QUESTIONS RE: THE RESUBMISSION
14-JAN-92	GENERAL CORRESP FROM FDA	OTHER N/A	FDA ACKNOWLEDGED RECEIPT OF RESUBMITTED NDA ON 31-DEC-91. NEW DUE DATE IS 28-JUN-92
21-JAN-92	PHONE CALL	OTHER N/A	CONSUMER SAFETY OFFICER REQUESTED ADDITIONAL COPIES OF CERTAIN VOLUMES
22-JAN-92	GENERAL CORRESP TO FDA	OTHER N/A	PROVIDED A NEW COPY OF THE SAS DATASETS OF EFFICACY & BLEEDING ASSESSMENT DATA FOR HIP REPLACEMENT SURGERY
24-JAN-92	GENERAL CORRESP TO FDA	OTHER N/A	PROVIDED DESK COPIES OF VOLUMES 77 AND 78

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 20164 Type: NDA
Route of Admin.: SU
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Dosage Form: SOLUTION 30 mg

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
28-JAN-92	GENERAL CORRESP TO FDA	OTHER N/A	PROVIDED FDA WITH A DESK COPY OF VOLUME 2.3
30-JAN-92	AMENDMENT	PRECLINICAL STUDY: SPECIES: RTE. ADMIN: DURATION:	RESPONSE TO THE QUESTIONS DR. AHMAD RAISED DURING HIS REVIEW OF NONCLINICAL DATA
04-FEB-92	PHONE CALL	CLINICAL PRO#: PAT NUM: 0 PAT INIT: PAT REACT: SRTYPE: Follow-up INV NAME:	CSO BRONNIE COLLIER STATED A SAFETY UPDATE WOULD NOT BE REQUIRED UNTIL THE APPLICATION APPROACHES APPROVABILITY
24-FEB-92	AMENDMENT	OTHER N/A	FOUR APPENDICES CONTAINING INFO REQUESTED BY FDA
24-FEB-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT
18-MAR-92	PHONE CALL	CMC Dos Form/Potency:	DRUG PRODUCT
19-MAR-92	AMENDMENT	LABEL/PRO MATERIAL FC NUM:	PACKAGE INSERT
19-MAR-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG PRODUCT
26-MAR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT
31-MAR-92	AMENDMENT	OTHER N/A	FDA'S RESPONSE TO STABILITY DATA RESPONSE TO 18-MAR-92 REQUEST FOR TWO DISKETTES OF PROPOSED PACKAGE INSERT REQUEST FOR INFORMATION RE: STABILITY DATA FOR EXPIRATION DATING RESPONSE TO 24-FEB-92 REQUEST FOR FURTHER INFORMATION RESPONSE TO FDA REQUEST FOR INFORMATION RE: CLINICAL STUDY ENO 884
01-APR-92	AMENDMENT	CLINICAL PRO#: 526 INV NAME:	STUDY RESPONSE TO 31-MAR-92 REQUEST FOR INFORMATION

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93 NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
App Num: 20164 Type: Dosage Form: SOLUTION 30 mg
Route of Admin.: SU
Generic Name: enoxaparin

CONTENT Name/Description		Content Comments	
COMM DATE	COMM TYPE	Details	
03-APR-92	GENERAL CORRESP From FDA	OTHER	N/A 31-MAR-92 SUBMISSION CONSIDERED MAJOR - EXTENDED DUE DATE TO 27-AUG-92
06-APR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT RESPONSE TO RECENT TELEPHONE REQUEST FOR SAMPLES OF SYRINGES AND BLISTER PACKAGES
08-APR-92	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT RESPONSE TO 19-MAR-92 FDA REQUEST FOR ADDITIONAL STABILITY INFORMATION TO SUPPORT PROPOSED EXPIRATION DATING
08-APR-92	GENERAL CORRESP To FDA	OTHER	N/A RESPONSE TO 02-APR-92 REQUEST FOR SPECIFIC INFO TO FACILITATE THE UPCOMING CLINICAL INVESTIGATOR INSPECTIONS IN CANADA
10-APR-92	GENERAL CORRESP To FDA	OTHER	N/A ADDITIONAL INFO REQUESTED 02-APR-92 RE: CASE REPORT FORMS FOR EN0884 AT HAMILTON GENL HOSP & HENDERSON GENL HOSPITALS
17-APR-92	GENERAL CORRESP To FDA	OTHER	N/A CONFIRMATION OF FDA INSPECTION DATE OF CLINICAL TRIAL EN0884 AT HENDERSON & HAMILTON HOSPITALS
21-APR-92	GENERAL CORRESP To FDA	OTHER	N/A RESPONSE TO 14-APR-92 FDA TELEPHONE CALL RE: PRE-APPROVAL INSPECTIONS FOR JULY OF 1992
01-MAY-92	GENERAL CORRESP To FDA	CMC Dos Form/Potency:	DRUG PRODUCT RESPONSE TO FDA REQUEST FOR INFORMATION
06-MAY-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG PRODUCT
	GENERAL CORRESP From FDA	CMC Dos Form/Potency:	DRUG SUBSTANCE
12-MAY-92	GENERAL CORRESP To FDA	CLINICAL PROB: INV NAME:	STUDY RESPONSE TO FDA REQUEST FOR INFORMATION RE: STATISTICAL ANALYSIS
15-MAY-92	PHONE CALL	CMC Dos Form/Potency:	DRUG PRODUCT FOLLOW-UP TO DISCUSSION ON CMC QUESTIONS

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93 App Num: 20164 Type: NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Route of Admin.: SU Dosage Form: SOLUTION 30 mg
Generic Name: enoxaparin

CONTENT Name/Description Details		Content Comments
COMM DATE	COMM TYPE	
20-MAY-92	PHONE CALL	N/A DISCUSS THE CMC, STABILITY AND REVIEW STATUS
02-JUN-92	PHONE CALL	CMC Dos Form/Potency: INJECTION 30 mg TO PROVIDE FDA'S STABILITY COMMITTEE' DECISION RE: TEMPERATURE AND TIME INTERVALS
11-JUN-92	PHONE CALL	OTHER N/A REVIEW STATUS UPDATE
16-JUN-92	GENERAL CORRESP From FDA	CMC Dos Form/Potency: INJECTION THREE REQUESTS RE: MICROBIOLOGICAL PORTION OF THE APPLICATION
17-JUN-92	PHONE CALL	CMC Dos Form/Potency: INJECTION 30 mg CONFERENCE CALL TO CLARIFY FDA REQUESTS FOR ADDITIONAL STABILITY INFO IN 06-MAY-92 LETTER
18-JUN-92	PHONE CALL	OTHER N/A FDA ADVISED EIAH DOES NOT FULLY MEET THE CRITERIA SPELLED OUT
19-JUN-92	AMENDMENT	CMC Dos Form/Potency: INJECTION RESPONSE TO 24-FEB-92 FDA LETTER PROVIDED REPRESENTATIVE TEST RESULTS & VALIDATION INFO
26-JUN-92	GENERAL CORRESP From FDA	OTHER N/A ACKNOWLEDGMENT OF RECEIPT OF 19-JUN-92 AND 24-FEB-92 AMENDMENTS. FDA EXTENDED THE DUE DATE TO 26-OCT-92
29-JUN-92	AMENDMENT	CMC Dos Form/Potency: PHARMACOKINETICS OTHER AMENDMENT TO A PENDING APPLICATION
14-JUL-92	PHONE CALL	N/A UPDATE OF APPLICATION STATUS FDA REQUESTED THAT WE SUBMIT SAFETY DATA UP TO AND INCLUDING 30-JUN-92
20-JUL-92	GENERAL CORRESP To FDA	CLINICAL PROB: INV NAME: STUDY RESPONSE TO FDA REQUEST FOR CONFIRMATION THAT EX VIVO STUDIES ON ENO84 PATIENTS DID NOT JEOPARDIZE THE BLINDING

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93	Drug Code: RP 54563	Trade Name: LOVENOX INJECTION
App Num: 20164	Type: NDA	
Route of Admin.: SU	Dosage Form: SOLUTION	
Generic Name: enoxaparin		30 mg

COMM DATE	COMN TYPE	CONTENT Name/Description Details	Content Comments
23-JUL-92	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	TO ASCERTAIN FDA'S POSITION REGARDING LOVENOX PACKAGING
06-AUG-92	PHONE CALL	OTHER	REQUEST FOR STATISTICAL ANALYSIS
07-AUG-92	GENERAL CORRESP TO FDA	OTHER	SELECTION OF LOVENOX AS THE TRADE NAME FOR MARKETING
11-AUG-92	GENERAL CORRESP TO FDA	OTHER	PROVIDED CORRECTED VERSIONS OF APPENDICES XIV, XV AND XVI
13-AUG-92	GENERAL CORRESP TO FDA	CMC Dos Form/Potency: INJECTION	RESPONSE TO 16-JUN-92 FDA REQUEST FOR INFORMATION
07-OCT-92	PHONE CALL	CMC Dos Form/Potency:	PROVIDED FDA WITH A STATUS UPDATE OF DR. TEMPLE'S REVIEW
10-NOV-92	FDA REPORT	SAFETY UPDATE	COVERING THE PERIOD 01-JAN-91 THROUGH 30-JUN-92
20-NOV-92	GENERAL CORRESP From FDA	LABEL/PRO MATERIAL FC NUM:	PROVIDE DRAFT LABELING
23-NOV-92	GENERAL CORRESP TO FDA	OTHER	RESPONSE TO APPROVALBE LETTER INTENT TO FILE AN AMENDMENT
24-NOV-92	GENERAL CORRESP TO FDA	OTHER	RESPONSE TO 20-NOV-92 REQUEST FOR ENVIRONMENTAL ASSESSMENT
08-DEC-92	GENERAL CORRESP TO FDA	LABEL/PRO MATERIAL FC NUM:	RESPONSE TO 20-NOV-92 FDA REQUEST FOR INFORMATION
11-DEC-92	PHONE CALL	OTHER	FOLLOWUP TO OUR DRAFT LABELING SUBMISSION OF 08-DEC-92
17-DEC-92	GENERAL CORRESP TO FDA	CMC Dos Form/Potency: INJECTION	RESPONSE TO FDA REQUEST FOR INFORMATION RE: STABILITY DATA FOR 30 MG PRODUCT
23-DEC-92	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	FDA REQUESTED REFERENCE TO ANTICOAGULANT ACTIVITY BE OMITTED FROM THE DESCRIPTION SECTION OF PI

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93 NDA Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
App Num: 20164 Type: Dosage Form: SOLUTION 30 mg
Route of Admin.: SU
Generic Name: enoxaparin

CONTENT Name/Description Details		Content Comments	
COMM DATE	COMM TYPE	DRUG PRODUCT	
24-DEC-92	GENERAL CORRESP TO FDA	CMC Dos Form/Potency:	RESPONSE TO 20-NOV-92 FDA LETTER
30-DEC-92	PHONE CALL	OTHER	STATUS REPORT OF NDA APPROVAL
08-JAN-93	GENERAL CORRESP TO FDA	LABEL/PRO MATERIAL FC NUM:	RESPONSE TO FDA REQUEST FOR INFORMATION RE: FINAL PRINTED LABELING
10-JAN-93	GENERAL CORRESP From FDA	CLINICAL PRO#: INV NAME:	STUDY
14-JAN-93	GENERAL CORRESP From FDA	OTHER	AMENDMENT CONSIDERED MAJOR - FDA EXTENDED REVIEW DUE DATE TO 25-APR-93
19-JAN-93	GENERAL CORRESP TO FDA	LABEL/PRO MATERIAL FC NUM:	PROVIDED DRAFT INTRODUCTORY PROMOTIONAL INFORMATION
19-JAN-93	PHONE CALL	OTHER	TO DISCUSS THE STATUS OF OUR APPLICATION IN GENERAL
25-JAN-93	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	TO OBTAIN CLARIFICATION OF LABELING
27-JAN-93	PHONE CALL	LABEL/PRO MATERIAL FC NUM:	TO DISCUSS THE INTRODUCTORY PROMOTIONAL LAUNCH CAMPAIGN MATERIAL
02-FEB-93	PHONE CALL	CMC Dos Form/Potency:	NDA STATUS UPDATE
09-FEB-93	PHONE CALL	CMC Dos Form/Potency:	RE: STATUS OF REVIEW
16-FEB-93	PHONE CALL	CLINICAL PRO#: INV NAME:	TO REVIEW W/DR. VINCENT SLIGHT MODIFICATIONS TO PROTOCOL SUBMITTED 29-JAN-92
17-FEB-93	PHONE CALL	OTHER	NDA STATUS UPDATE
19-FEB-93	GENERAL CORRESP TO FDA	CMC Dos Form/Potency:	RESPONSE TO 15-JAN-93 REQUEST RE: CONTAMINATION TESTING OF DISTILLED WATER

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 20164 Type: NDA
Route of Admin.: SU
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: LOVENOX INJECTION
Dosage Form: SOLUTION 30 mg

CONTENT Name/Description		Content Comments	
COMM DATE	COMM TYPE	Details	
23-FEB-93	GENERAL CORRESP To FDA	CMC Dos Form/Potency: INJECTION	DRUG PRODUCT RESPONSE TO 15-JAN-93 FDA REQUEST FOR INFORMATION
10-MAR-93	GENERAL CORRESP From FDA	SAFETY UPDATE	FDA REQUESTS ADDITIONAL INFORMATION RE: 10-NOV-92 SAFETY UPDATE
29-MAR-93	GENERAL CORRESP From FDA	OTHER	APPROVAL LETTER
31-MAR-93	GENERAL CORRESP To FDA	LABEL/PRO MATERIAL FC NUM:	PROVIDED AN ADDITIONAL PIECE FOR THE INTRODUCTORY PROMOTIONAL LAUNCH CAMPAIGN INFORMATION
09-APR-93	GENERAL CORRESP From FDA	LABEL/PRO MATERIAL FC NUM:	FDA COMMENTS AFTER REVIEW OF INTRODUCTORY PROMOTIONAL MATERIALS

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APPLICATION CHRONOLOGY REPORT
Report Cover Page

Run Date: 05/05/93

User: ingres_prod

Selection Criteria

App Number:

31532

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Regulatory Affairs**

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND
Route of Admin.: IV
Generic Name: enoxaparin

Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Dosage Form: INJECTION
100 mg/mL

CONTENT Name/Description		Content Comments	
COMM DATE	COMM TYPE	Details	
18-APR-88	ORIGINAL SUBMISSION	OTHER	N/A ORIGINAL SUBMITTED
19-MAY-88	GENERAL CORRESP From FDA	OTHER	N/A EFFECTIVE DATE OF IND
03-DEC-90	AMENDMENT	OTHER	N/A PRE-NDA MEETING REQUEST
15-JAN-91	AMENDMENT	OTHER	N/A REQUEST FOR PRE-NDA MEETING
17-JAN-91	AMENDMENT	OTHER	N/A RPR NOTIFICATION OF TRANSFER OF OWNERSHIP OF IND TO RHONE-POULENC RORER 31-JUL-90
17-JAN-91	AMENDMENT	OTHER	N/A RPP TRANSFER OF OWNERSHIP OF IND TO RHONE-POULENC RORER ON 31-JUL-90
06-FEB-91	GENERAL CORRESP From FDA	OTHER	N/A FDA REQUEST FOR INFO TO COMPLETE THE CHANGE IN OWNERSHIP
01-MAR-91	AMENDMENT	OTHER	N/A CONFIRMATION OF PRE-NDA MEETING & AGENDA
14-MAR-91	MEETING MINUTES	OTHER	N/A PRE-NDA MEETING OVERVIEW
25-APR-91	AMENDMENT	CLINICAL PRO#: INV NAME:	STUDY RESPONSE TO 21-AUG-89 FDA LETTER
	AMENDMENT	CMC Dos Form/Potency:	DRUG PRODUCT RESPONSE TO 21-AUG-89 FDA LETTER
15-MAY-91	AMENDMENT	OTHER	N/A RESPONSE TO 06-FEB-91 FDA LETTER RE: ADDITIONAL INFO ON TRANSFER OF OWNERSHIP
24-JUL-91	FDA REPORT	ANNUAL RPT	N/A COVERING THE PERIOD 19-MAY-90 THROUGH 18-MAY-91
14-AUG-91	AMENDMENT	CLINICAL PRO#: INV NAME:	STUDY RESPONSE TO 21-AUG-89 FDA LETTER
15-OCT-91	AMENDMENT	OTHER	N/A CHANGE OF ADDRESS

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND
Route of Admin.: IV
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Dosage Form: INJECTION 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
14-NOV-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: OVERDYKE, WILLIAM L RITTER, MERRILL	STUDY
21-NOV-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: COMP, PHILIP C	STUDY
22-NOV-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: GECKLER, RONALD W	STUDY
25-NOV-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: JOHNSON, GERHARD	STUDY
02-DEC-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: ZIMMERMAN, RICHARD	STUDY
09-DEC-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: FURMAN, W KIM	STUDY
11-DEC-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: KIM, HUGH C	STUDY
17-DEC-91	AMENDMENT	CLINICAL PRO#: 547 INV NAME: MATHEES, DONALD J	STUDY
06-JAN-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: BLAHA, J DAVID BONA, ROBERT D TROWBRIDGE, ARTHUR A	STUDY
08-JAN-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: WISE, GREGORY	STUDY

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND
Route of Admin.: IV
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Dosage Form: INJECTION 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
23-JUL-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: YOUNG, TIMOTHY STUDY	
23-JUL-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: MERLI, GENO J STUDY	
28-JUL-92	FDA REPORT	ANNUAL RPT N/A	COVERING THE PERIOD 19-MAY-91 THROUGH 18-MAY-92
12-AUG-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: TROWBRIDGE, ARTHUR A STUDY	
14-AUG-92	AMENDMENT	CLINICAL PROJ: 547 INV NAME: WINTERS, THOMAS F STUDY	
24-AUG-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: OVERDYKE, WILLIAM L STUDY	
26-AUG-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: JOHNSON, WILLIAM M STUDY	
02-SEP-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: TREMAINE, M DAVID STUDY	
08-SEP-92	AMENDMENT	CLINICAL PROJ: 547 INV NAME: MANNAL, RICHARD STUDY	
08-SEP-92	AMENDMENT	CLINICAL PROJ: 569 INV NAME: HAIRE, WILLIAM D STUDY	
22-SEP-92	AMENDMENT	CLINICAL PROJ: 124 INV NAME: FURMAN, W KIM STUDY	

US00468 CARLTON SAVORY NOT IN SPIN

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND
Route of Admin.: IV
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Dosage Form: INJECTION 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
15-JAN-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: GONZALES, FRANCISCO WHITSETT, THOMAS	STUDY
31-JAN-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: ALEDORT, LOUIS	STUDY
24-FEB-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: COMEROTA, ANTHONY J	STUDY
09-MAR-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: COLWELL, CLIFFORD	STUDY
10-MAR-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: BONA, ROBERT D	BURROUGHS, M.D.; SUSAN IS LISTED AS AN INVESTIGATOR BUT NOT IN SPIN 26-MAR-92
17-MAR-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: LYONS, ROGER M	STUDY
23-MAR-92	AMENDMENT	CLINICAL PRO#: 547 INV NAME: ECONOMIDES, NICHOLAS	STUDY
01-JUL-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME: YOUNG, TIMOTHY	STUDY
02-JUL-92	AMENDMENT	CLINICAL PRO#: 127 INV NAME: SICA, DOMENIC A	STUDY GEHR, TODD W.B.; AND RIPLEY, ELIZABETH D. ARE CO-INVESTIGATORS
16-JUL-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME: CHRISTIE, MICHAEL GUSTILO, RAMON O'DONNELL, DENIS M	STUDY

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93
App Num: 31532 Type: IND
Route of Admin.: IV
Generic Name: enoxaparin
Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
Dosage Form: INJECTION 100 mg/mL

COMM DATE	COMM TYPE	CONTENT Name/Description Details	Content Comments
07-OCT-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME: STULBERG, BERNARD	STUDY
08-OCT-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME: FURMAN, W KIM	STUDY
20-OCT-92	FDA REPORT	CLINICAL PRO#: 569 INV NAME: BERNASEK, THOMAS L	CO-INVESTIGATOR WILLIAM R. KENNEDY
11-NOV-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME:	US00465 FITZGERALD, ROBERT H., NOT IN SPIN 10-NOV-92
07-DEC-92	AMENDMENT	CLINICAL PRO#: 569 INV NAME:	CURTISS MULL IS NOT IN SPIN
21-DEC-92	AMENDMENT	INVEST IND N/A	EDWARDS, RICHARD L, THE SCHOOL OF MEDICINE OF THE UNIVERSITY OF CONNECTICUT, 263 FARMINGTON, FARMINGTON, CT 06030
12-JAN-93	AMENDMENT	CLINICAL PRO#: 569 INV NAME: FISHER, DAVID A	STUDY
19-JAN-93	AMENDMENT	CLINICAL PRO#: 569 INV NAME: WINTERS, THOMAS F	STUDY
26-JAN-93	AMENDMENT	CLINICAL PRO#: 569 INV NAME: GECKLER, RONALD W RITTER, MERRILL	STUDY
11-FEB-93	AMENDMENT	CLINICAL PRO#: 569 INV NAME: LEDES, CLAUDE P	STUDY

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APPLICATION CHRONOLOGY REPORT

Run Date: 05/05/93 IND Drug Code: RP 54563 Trade Name: TO BE ASSIGNED
App Num: 31532 Type: Dosage Form: INJECTION 100 mg/mL
Route of Admin.: IV
Generic Name: enoxaparin

CONTENT Name/Description		Content Comments
COMM DATE	COMM TYPE	
01-MAR-93	AMENDMENT	
	CLINICAL	STUDY
	PROB:	569
	INV NAME:	BERNASEK, THOMAS L
		WHITSETT, THOMAS